

REMARKS

The Office Action and the Advisory Action have been carefully reviewed. No claim is allowed. Claims 1, 3, 5-12, 17, 18, and 22-25 presently appear in this application and define patentable subject matter warranting their allowance.

Reconsideration and allowance are hereby respectfully solicited.

Claim 19 is cancelled and claim 1 is now amended to recite that the bond between the spacer and a carboxyl group of hyaluronic acid is an amide bond.

The examiner has indicated in the Advisory Action of October 15, 2004, that, while the priority date is perfected by the English translation of the foreign priority documents, the previous §102(b) rejection would become a §102(e) rejection. Regarding this new issue under §102(e) and the rejections under §103(a) which rely on the cited Prestwich reference, applicants provide their comments as follows:

The presently claimed invention is neither anticipated by Prestwich nor suggested by Prestwich in combination with other secondary references. Prestwich discloses a conjugate (HA-CO-NH-NH-...) which is formed by reacting a hydrazine group with a carboxyl group of hyaluronic acid (See claim 1 and the examples of Prestwich).

By contrast, the presently claimed invention relates to a conjugate (HA-CO-NH-... e.g., HA-CO-NH-CH₂-) which is formed by

reacting an amino group of a spacer with a carboxyl group of hyaluronic acid (See the present specification, page 34, lines 1 to 14 and Examples 2 to 8, pages 48-55). The hydrazine group used to form the conjugate (HA-CO-NH-NH-...) in Pestwisch is quite different from the amino group used to form the conjugate (HA-CO-NH-...) recited in the present claims, as discussed below.

(1) Re: Classification

The hydrazine and amino groups are classified into separate categories according to IUPAC nomenclature as shown in the attached sheets. The amino group is classified into "C-8 Groups Containing One Nitrogen Atom" while the hydrazine group is classified into "C-9 Groups Containing More Than One Nitrogen Atom".

(2) Re: Reactivity with carbonyl

The amino group reacts with a carbonyl group to form an imine which is unstable and subject to hydrolysis. By contrast, the hydrazine group reacts with a carbonyl group to form hydrazone which crystallizes, is stable, and is often used in purification and identification of aldehydes and ketones. Imine is hardly ever purified. Thus, the conjugate (HA-CO-NH-... e.g. HA-CO-NH-CH²-) of the present invention is quite different from the conjugate (HA-CO-NH-NH-...) disclosed in Prestwisch and cannot be anticipated by Prestwisch or made obvious from Prestwisch in

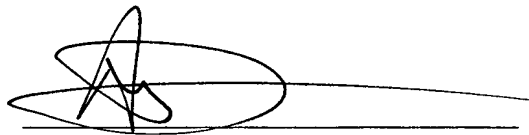
Appln. No. 09/700,879
Amd. dated November 1, 2004
Reply to Office Action of October 15, 2004

combination with the disclosures and teachings of the secondary references.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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Recommendations 1979

C. Characteristic Groups Containing Carbon, Hydrogen, Oxygen, Nitrogen, Halogen, Sulfur, Selenium, and/or Tellurium

 Preface of Second Edition of Section C

 Preamble

 C-0. Nomenclature Systems

 Preamble to Subsections C-1 to C-9

 C-1 Halogen Derivatives

 C-2 Alcohols, Phenols, and Their Derivatives

 C-3 Aldehydes, Ketones, and Their Derivatives

 C-4 Carboxylic Acid and Their Derivatives

 C-5 Compounds Containing Bivalent Sulfur

 C-6 Sulfur Halides, Sulfoxides, Sulfones, and Sulfur Acids and Their Derivatives

 C-7 Compounds Containing Selenium or Tellurium Linked to an Organic Radical

 C-8 Groups Containing One Nitrogen Atom

 C-9 Groups Containing More Than One Nitrogen Atom

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Recommendations 1979



C. Characteristic Groups Containing Carbon, Hydrogen, Oxygen, Nitrogen, Halogen, Sulfur, Selenium, and/or Tellurium



C-8 Groups Containing One Nitrogen Atom

- ☐ 8.1 Amines
- ☐ 8.2 Amides and Imides
- ☐ 8.3 Nitriles, Isocyanides, and Their Derivatives
- ☐ 8.4 Hydroxylamines and Their Derivatives
- ☐ 8.5 Nitroso and Nitro Compounds
- ☐ 8.6 Amine Radical Ions



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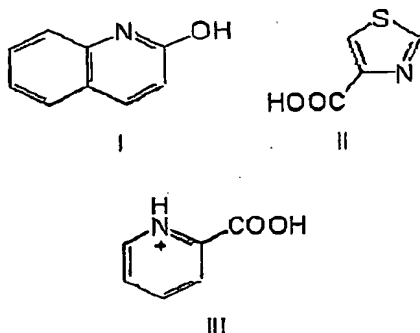
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Groups Containing One Nitrogen Atom

Amines Rule C-811 General

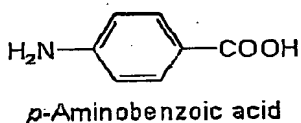
811.1 – Bases in which nitrogen forms part of a ring are named as heterocyclic compounds in accordance with Section B of these Rules. The termination “-ine”, “-ole”, or “-ete” of such names is not considered to be a suffix in the sense of Rule C-10.3, and so may be followed by endings to denote a substituent of the heterocycle, as, for example, in 2-quinolinol (I) or 4-thiazolecarboxylic acid (II). However, the endings denoting quaternary atoms (see Rule C-816) are considered as suffixes, and substituents must then be named by prefixes, as, for example, in 2-carboxypyridinium chloride (III). In the same way as “-ium” the ending “-amine” (see below) is considered as a suffix.



811.2 – The generic name “amine” is applied to compounds NH_2R , NHR^1R^2 , and $\text{NR}^1\text{R}^2\text{R}^3$, which are called primary, secondary, and tertiary amines, respectively. In a wider sense, compounds containing nitrogen in a ring and owing their basicity to this atom may also be referred to as “amines”.

811.3 – An -NH_2 group, when not the principal group, is named by the prefix “amino-”.

Examples to Rule C-811.3



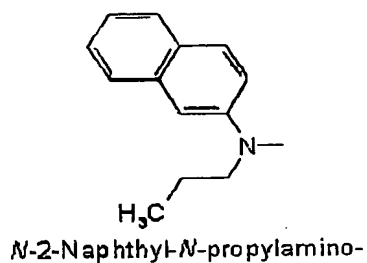
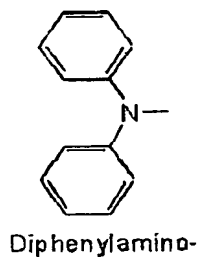
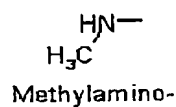
Note: In Beilstein's *Handbuch der organischen Chemie* use of the prefix “amino-” is permitted as an alternative, when -NH_2 is the principal group, but this method is not recommended here; it leads to names such as 1-aminobutane, 2-aminopentane, and 1-aminoanthracene.

811.4 – Radicals $\text{RNH}\cdot$, $\text{R}_2\text{N}\cdot$, and $\text{R}^1\text{R}^2\text{N}\cdot$ are named as substituted amino groups by changing “ine” of the amine to “ino”.

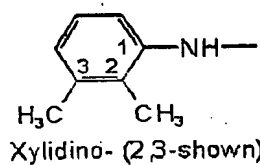
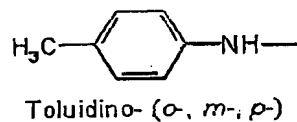
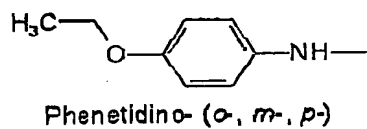
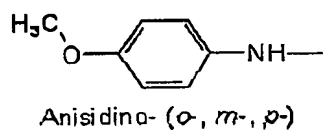
Examples to Rule C-811.4

Rule C-811 Amines. General (Groups Containing One Nitrogen Atom)

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The following are examples of trivial names which are retained:



See Recommendations'93 R-5.4

Rule C-811 Amines. General (Groups Containing One Nitrogen Atom)

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Next:

Amines C-812, C-813, C-814, C-815, C-816Amides and Imides C-821, C-822, C-823, C-824, C-825, C-826, C-827Nitriles, Isocyanides, and Their Derivatives C-831, C-832, C-833, C-834Hydroxylamines and Related Compounds C-841, C-842, C-843Nitroso and Nitro Compounds C-851, C-852Amine Radical Ions C-861

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Recommendations 1979



C. Characteristic Groups Containing Carbon, Hydrogen, Oxygen, Nitrogen, Halogen, Sulfur, Selenium, and/or Tellurium



C-9 Groups Containing More Than One Nitrogen Atom

- ☐ C-9 Introduction
- ☐ 9.1 Azo and Azoxy Compounds
- ☐ 9.2 Hydrazines and Their Derivatives
- ☐ 9.3 Diazonium and Related Groups
- ☐ 9.4 Groups Containing Three or More Contiguous Nitrogen Atoms
- ☐ 9.5 Compounds Containing a N=C-N or N=C=N Group
- ☐ 9.6 Compounds Containing a N-C(-N)=N Group
- ☐ 9.7 Compounds Containing a N-CO-N or Related Group
- ☐ 9.8 Compounds Containing a N-CO-N-N or More Complex Group



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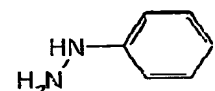
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Hydrazines and Their Derivatives

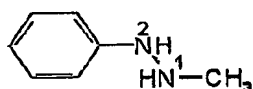
Rule C-921

921.1 – Compounds derived by replacement of hydrogen in hydrazine by groups other than acyl (for which see Rule C-921.5) are named (a) as substitution products of hydrazine or (b), if a group having priority for citation as principal group is also present, by use of the prefix “hydrazino-”. The nitrogen atoms are denoted by locants *N* and *N'*, or 1 and 2. For method (a) numerical locants are the lowest possible, or primes as few as possible; for method (b) the nitrogen atom at the point of attachment is unprimed or has locant 1.

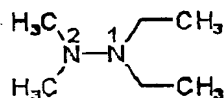
Examples to Rule C-921.1



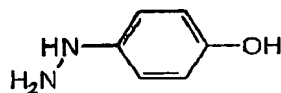
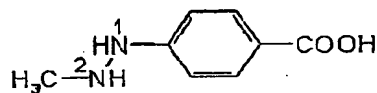
Phenylhydrazine



N-Methyl-*N'*-phenylhydrazine
or 1-Methyl-2-phenylhydrazine



N,N-Diethyl-*N',N'*-dimethylhydrazine
or 1,1-Diethyl-2,2-dimethylhydrazine

*p*-Hydrazinophenol

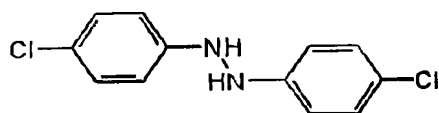
p-(*N'*-Methylhydrazino)benzoic acid
or *p*-2-Methylhydrazinobenzoic acid

921.2 – Alternatively, for compounds $R^1NH-NHR^2$ in which the radicals R^1 and R^2 are derived from parent molecules that, when unsubstituted, are identical, names may be formed by methods analogous to those used for azo compounds (Rules C-911 and C-912) but with “hydrazo” in place of “azo”. The names so obtained are available for indication of further substitution on the nitrogen atoms provided that no ambiguity is caused thereby; when ambiguity would be caused thereby, the compounds are named according to Rule C-921.1.

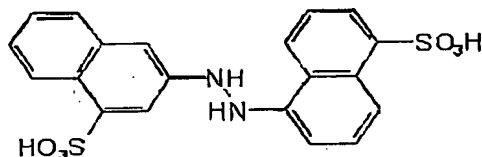
Examples to Rule C-921.2

Rule C-921 (Hydrazines and Their Derivatives)

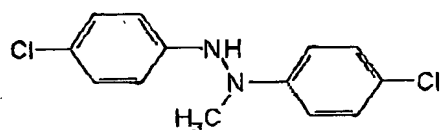
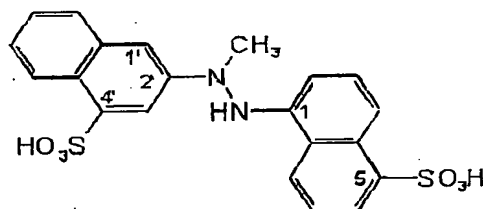
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4,4'-Dichlorohydrazobenzene

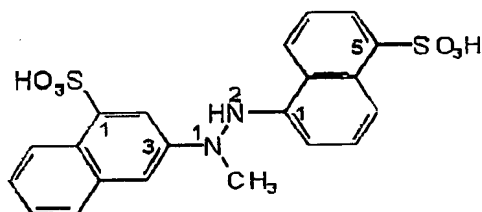


1,2'-Hydrazonaphthalene-4',5-disulfonic acid
(compare Rule C-911.1)
or 3,5'-Hydrazodi-(1-naphthalenesulfonic acid)
(compare Rule C-912.2)

4,4'-Dichloro-*N*-methylhydrazobenzene

N'-Methyl-1,2'-hydrazonaphthalene-4',5-disulfonic acid
(compare Rule C-911)

or



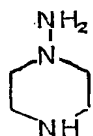
3-[1-Methyl-2-(5-sulfo-1-naphthyl)hydrazino]-
1-naphthalenesulfonic acid
(compare Rule C-912)

921.3 – When one nitrogen atom of a hydrazine group forms part of a ring the compound is named as an amino derivative of the heterocycle.

Example to Rule C-921.3

Rule C-921 (Hydrazines and Their Derivatives)

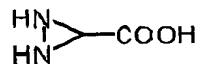
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1-Aminopiperazine

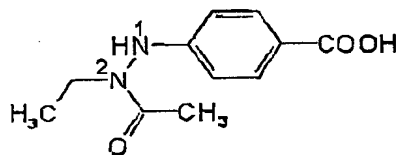
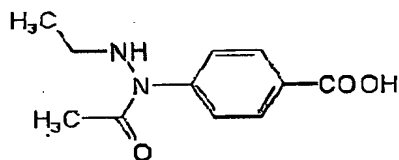
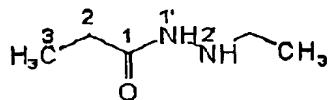
921.4 – A group -NH-NH- attached to a single carbon atom is denoted by a prefix “hydrazin-” when another group having priority for citation as principal group is also present. See, however, Rule B-1.

Example to Rule C-921.4

Hydraziaacetic acid
or Diaziridine-3-carboxylic acid

921.5 – Compounds formed by replacement of hydrogen of a hydrazine group by an acyl group, and their further substitution products, are named by one of the following methods: (a) If a substituent having priority for citation as principal group is also present, the compound is named as an acylhydrazino compound (compare Rule C-921.1); the nitrogen atom attached to the parent carrying the principal group has the locant N (unprimed) or 1. (b) If there is no substituent having priority for citation as principal group, the ending “ic acid” or “-oic acid” of the name of the acid is changed to “-ohydrazide”; or if the ending of the name of the acid is “-carboxylic acid”, this is changed to “-carbohydrazide”; the nitrogen atom attached to the acyl group then has the locant *N* or 1’.

Examples to Rule C-921.5

*p*-(*N'*-Acetyl-*N'*-ethylhydrazino)benzoic acid
or *p*-(2-Acetyl-2-ethylhydrazino) benzoic acid*p*-(*N*-Acetyl-*N'*-ethylhydrazino)benzoic acid
or *p*-(1-Acetyl-2-ethylhydrazino) benzoic acid*N'*-Ethylpropionohydrazide
or 2'-Ethylpropionohydrazide

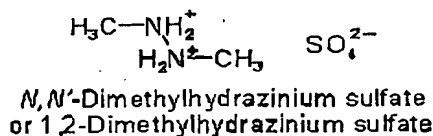
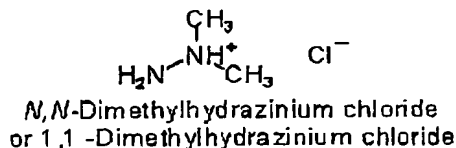
921.6 – Salts of hydrazines are named as derivatives of hydrazinium(1+) or hydrazinium(2+),

Rule C-921 (Hydrazines and Their Derivatives)

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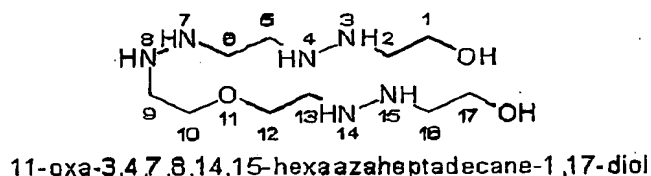
according to whether one or both nitrogen atoms bear a charge (see Rule 3.17 of I.U.P.A.C. *Nomenclature of Inorganic Chemistry*, 1970 ²). If only one nitrogen atom bears a charge and it is known which, then that atom has the locant *N* (unprimed) or 1.

Examples to Rule C-921.6



921.7 – Acyclic polyhydrazines may be named by replacement nomenclature (see Subsection C-0.6).

Example to Rule C-921.7



See Recommendations '93 R-5.6.6, R-5.7.8.4

Next:

Hydrazines and Their Derivatives C-922, C-923

Diazonium and Related Groups C-931

Groups Containing Three or More Contiguous Nitrogen Atoms C-941, C-942

Compounds Containing a N=C-N or N=C=N Group C-951, C-952, C-953, C-954, C-955, C-956

Compounds Containing a N-C(-N)=N Group C-961, C-962

Compounds Containing a N-CO-N or Related Group C-971, C-972, C-973, C-974, C-975

Compounds Containing a N-CO-N-N or More Complex Group C-981, C-982, C-983, C-984, C-985



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